

invention identifies that G $\alpha$ 14, a G-protein alpha subunit, is specifically and selectively expressed in taste receptor cells. This gene was found to be co-expressed with G-protein coupled taste receptors, GPCR-B3 and GPCR-B4 (*see* USSN 09/361,652, filed July 27, 1999 and USSN 09/361,631, filed July 27, 1999, now US Patent 6,383,778). These taste receptors have been previously shown to be expressed in topographically distinct subpopulations of taste receptor cells and taste buds. These receptors are specifically localized to the taste pore, and are distantly related to putative mammalian pheromone receptors. The present invention thus demonstrates that G $\alpha$ 14 is specifically expressed in taste cells and further that it is co-expressed with GPCR-B3 and GPCR-B4 receptors in the different taste papillae. The G-protein alpha subunits that are specifically expressed in taste cells can thus be used, e.g., to screen for modulators of taste. The compounds identified by these assays would then be used by the food and pharmaceutical industries to customize taste, e.g., as additives to food or medicine so that the food or medicine tastes different to the subject who ingests it. For example, bitter medicines can be made to taste less bitter, and sweet substance can be enhanced.

Please amend the specification on page 11, lines 30-31:

“TC-GPCR” refers to a G-protein coupled receptor that is specifically expressed in taste receptor cells such as foliate, fungiform, and circumvallate cells. Such taste cells can be identified because they express molecules such as Gustducin, a taste cell specific G-protein (McLaughlin *et al.*, *Nature* 357:563-569 (1992)). Taste receptor cells can also be identified on the basis of morphology (*see, e.g.,* Roper, *supra*). Examples of TC-GPCR include GPCR-B3 and GPCR-B4 (*see, e.g.,* Hoon *et al.*, *Cell* 96:541-551 (1999); *see also* USSN 09/361,652, filed July 27, 1999 and USSN. 09/361,631, filed July 27, 1999, now US Patent 6,383,778), herein incorporated by reference in their entirety). TC-GPCRs encode G-protein coupled receptors with seven transmembrane regions that have “G-protein coupled receptor activity,” as described below, e.g., they bind to G-proteins in response to extracellular stimuli and promote

production of second messengers such as IP<sub>3</sub>, cAMP, and Ca<sup>2+</sup> via stimulation of enzymes such as phospholipase C and adenylate cyclase (for a description of the structure and function of G-protein coupled receptors, see, e.g., Fong, supra, and Baldwin, supra).

Please amend the specification on page 32, lines 26-27:

In a preferred embodiment, TC-G $\alpha$ <sub>14</sub> activity is measured by expressing TC-G $\alpha$ <sub>14</sub> in a heterologous cell with a TC-GPCR (*see* USSN 09/361,652, filed July 27, 1999 and USSN 09/361,631, filed July 27, 1999, now US Patent 6,383,778). As shown in Example I below, TC-G $\alpha$ <sub>14</sub> is specifically expressed in taste receptor cells, and also co-expressed with GPCR-B3 and GPCR-B4, in different taste papillae. As described above, HEK-293 cells may be used as a heterologous host cell, and modulation of taste transduction is assayed by measuring changes in intracellular Ca<sup>2+</sup> levels.

Please amend the specification on page 59, lines 28-29:

These experiments demonstrate that G $\alpha$ <sub>14</sub> is specifically and selectively expressed in circumvallate, foliate and fungiform taste receptor cells of the tongue, as shown by *in situ* hybridization. Therefore, G $\alpha$ <sub>14</sub> is a G alpha subunit that is specifically expressed in taste receptor cells. Furthermore, this gene is co-expressed with both GPCR-B3 and GPCR-B4 receptors in the different taste papillae (*see* USSN 09/361,652, filed July 27, 1999 and USSN. 09/361,631, filed July 27, 1999, now US Patent 6,383,778).

#### IN THE CLAIMS

Please amend claims 1 and 6 as follows.

1. (twice amended) A method for identifying a compound that modulates signal transduction in taste cells, the method comprising the steps of:

(i) contacting a cell which expresses a taste cell specific G-protein alpha subunit polypeptide and a taste cell specific G protein coupled receptor with the compound, the G-protein alpha subunit polypeptide comprising greater than 70% amino acid sequence identity to a polypeptide having a sequence of SEQ ID NO:2; and

(ii) determining a functional effect of the compound upon the cell expressing the G-protein alpha subunit polypeptide and the taste cell specific G protein coupled receptor, thereby identifying a compound that modulates signal transduction in taste cells.

6. (once amended) The method of claim 1, wherein the functional effect is determined by measuring increased or decreased binding of radiolabeled GTP to the G-protein alpha subunit polypeptide or to a G protein comprising the G-protein alpha subunit polypeptide.

#### **REMARKS**

Claims 1-4 and 6-8 are pending in the application and have been examined. The rejections are addressed below in the order raised by the Examiner. Appendix A provides the "Version with Markings to Show Changes Made." All pending claims are provided in Appendix B for the Examiner's convenience.

#### **Objection to the specification**

The specification was objected to for referencing two patent applications, and an updated status was requested. The specification has been amended to update the status of the applications (one pending, one issued). Applicants respectfully request that the objection be withdrawn.